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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/583,042	05/30/00	LEE T	TSRI609.1

HM12/1219

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EXAMINER	
RUSSEL, J	
ART UNIT	**PAPER NUMBER**
1653	5

DATE MAILED: 12/19/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/581,044	Applicant(s) T. Lee et al
	Examiner J. Russel	Group Art Unit 1653

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 8-11-2000 and 10-23-2000.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☒ Claim(s) 1-22 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-6, 8, 10-12, and 14 is/are rejected.

☒ Claim(s) 7, 9, 13, and 15-22 is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosur Statement(s), PTO-1449, Paper No(s). _____

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Oth r _____

Office Action Summary

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons:

Amino acid and nucleotide sequences are set forth, e.g., at page 13, line 3; page 25, line 26 - page 26, line 1; page 33, line 10; page 34, lines 5-7; page 59, line 27 - page 60, line 1; page 60, lines 22-23; page 61, line 27; and page 62, lines 3, 10, and 19; of the specification. However, no sequence listing has been submitted. Further, SEQ ID NOS need to be inserted after each sequence subject to the sequence disclosure rules. See 37 CFR 1.821(d).

Applicant must provide an original computer readable form (CRF) copy of the Sequence Listing, an original paper copy of the Sequence Listing as well as an amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and include no new matter as required by 37 CFR 1.825(a) and (b).

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

3. Claims 6 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. Claims 6 and 8 use "R^3" and "R^4" to define substituents which are different than the substituents defined by "R^3" and "R^4" in the independent claim. The same label can not be used to define different substituents in the claims.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

5. Claim 1 is rejected under 35 U.S.C. 103(a) as being obvious over the European Patent Application '145. The European Patent Application '145 teaches an HIV-protease inhibitor at column 3, lines 25-32, and page 10, lines 1-19, which differs from Applicant's claimed protease inhibitors in that the European Patent Application '145, for the compound of page 10, does not specifically teach X being methylene, R_{21} and R_{22} being H, and R_3 being t-butyl, although these possibilities are embraced by the generic formula at page 3. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to form a compound according to the European Patent Application '145 in which X is methylene, R_{21} and R_{22} are H, and R_3 is t-butyl, because these possibilities are embraced by the generic formula, because the choice of X being methylene and R_{21} and R_{22} being H results in the presence of a conventional proline residue, because the choice of R_3 being t-butyl is the choice of homologous small alkyl groups, and because the resulting compound has only the expected protease inhibitory activity.

6. Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application '361. The WO Patent Application '361 at claims 1 and 2 teaches a protease inhibitor which has the same structure as the compound recited in Applicant's claim 2.

7. Claim 2 is rejected under 35 U.S.C. 103(a) as being obvious over Baker et al. Baker et al teach an HIV-protease inhibitor at column 1, lines 53-64 and column 2, lines 1-17, which differs from Applicant's claimed protease inhibitors in that Baker et al, for the compound of column 2, does not specifically teach n=0, R_2 and R_{2a} being carbobenzoxy, and R_1 being the sidechain for valine, although these possibilities are embraced by the generic formula at claim 1. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to form a compound according to Baker et al in which n=0, R_2 and R_{2a} are carbobenzoxy, and R_1 is the sidechain for valine, because these possibilities are embraced by the generic formula, because n=0 is one of only two possibilities for n and is the possibility present in the more preferred embodiment at column 2, formula 3, because carbobenzoxy is a conventional N-blocking group, because the choice of R_1 being the sidechain for valine is the choice for homologous small alkyl groups and is the possibility present in the more preferred embodiment at column 2, formula 3, and because the resulting compound has only the expected protease inhibitory activity.

8. Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by the Dreyer et al article. The Dreyer et al article at page 941, Table II, teaches protease inhibitors which have the same structure as the compound recited in Applicant's claim 2.

9. Claim 2 is rejected under 35 U.S.C. 103(a) as being obvious over Kempf et al. Kempf et al teach an HIV-protease inhibitor at column 2, line 39 - column 6, line 50, and at claim 4 which differs from Applicant's claimed protease inhibitors in that Kempf et al, for the compound of claim 4, has a heterocyclic group rather than a phenyl group at R_7, although this possibility is embraced by the generic formula at column 4, line 67 - column 5, line 4. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to form a compound according to Kempf et al in which in the compound of claim 4, R_7 is phenyl, because this possibility is embraced by the generic formula, because carbobenzoxy is a conventional N-blocking group, and because the resulting compound has only the expected protease inhibitory activity.

10. Claim 3 is rejected under 35 U.S.C. 103(a) as being obvious over Handa et al. Handa et al at Examples 15 and 85 teach compounds which have the same structure as the compound recited in Applicant's claim 3, except that Handa et al's compounds comprise asparagine and cysteine residues rather than a valine residue. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the compounds of Handa et al with a valine residue rather than an asparagine or cysteine residue, because Handa et al disclose an alkyl sidechain to also be a preferred substituent at the same position as the asparagine sidechain (see column 5, lines 14-16), because valine is also a commonly available and well-known amino acid, and because the resulting compound has only the expected protease inhibitory activity.

11. Claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by Thompson et al. Thompson et al at column 2, lines 31-48, and column 7, lines 26-39 teaches protease inhibitors which have the same structure as the compound recited in Applicant's claim 4.

12. Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Tien et al. Tien et al at column 4, lines 1-15, teaches a protease inhibitor which has the same structure as the compound recited in Applicant's claim 5.

13. Claims 1, 6, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by the Tam et al article. The Tam et al article teaches compound 3 (see Table I) which corresponds to Applicants' compounds of claims 1 and 6 in which R_1 is carbobenzoxy, R_2 is CH_2-Phenyl, and R_4 is -H(t-Butyl). The Tam et al article teaches compound 7 (see Table I) which corresponds to Applicants' compounds of claims 1 and 8 in which R_1 is carbobenzoxy-valine-, R_2 is CH_2-Phenyl, and R_4 is -H(t-Butyl).

14. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application '100. The WO Patent Application '100 teaches compounds 17-R and 18-S (see page 49) which correspond to Applicants' compounds of claim 1 in which R_1 is carbobenzoxy, R_2 is CH_2-Phenyl, R_3 and R_4 are hydrogen or hydroxyl, R_5 and R_6 are a single combined oxygen forming a carbonyl group, and R_8 is -H(t-Butyl).

15. Claims 2, 10, and 11 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application '948. The WO Patent Application '948 teaches compounds 9 and 108 (see page 32) which differ from Applicants' claimed compounds in that the amino acid residue in the

WO Patent Application '948 in the second and second-to-last position of each compound is Ala rather than Val. The WO Patent Application '948 teaches in general that both Ala and Val can be used in these sections of the compounds, designated by the reference as $(B)_n$ (see page 3, lines 1-8). It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form compounds according to the WO Patent Application '948 which have the structure of compounds 9 and 148 except that Val rather than Ala is present in the second and second-to-last positions of each compound, because such compounds are generically embraced by the WO Patent Application '948, because the substitution of valine for alanine is a conservative substitution of amino acids and a homologous substitution of amino acid sidechains which would not have been expected to materially affect the activity of the compounds, and because the resultant compounds have only the HIV protease inhibitory activity which would have been expected in view of the WO Patent Application '948 (see, e.g., page 31).

16. Claims 2 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Jadhav et al. Jadhav et al teach compounds of Examples 91 and 93 (see columns 83-86) which correspond to Applicants' compounds of claim 2 and 10 in which R_1 is carbobenzoxy-glycine-valine- or carbobenzoxy-leucine-valine, and R_2 is CH_2-Phenyl. Jadhav et al's compounds are deemed inherently to have the same stereochemistry as Applicants' claimed compounds because of their similarity in activity, i.e. they all inhibit HIV proteases (see, e.g., column 2, lines 8-30 of Jadhav et al). Alternatively, to the extent that Jadhav et al's syntheses may produce stereochemical

mixtures, such mixtures anticipate Applicants' claimed compounds because Applicants' claims do not require the compounds to be stereochemically pure.

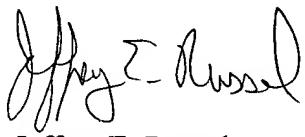
17. Claim 11 is rejected under 35 U.S.C. 103(a) as being obvious over Jadhav et al. Application of Jadhav et al is the same as in the above rejection of claims 2 and 10. Jadhav et al's compounds differ from the compound of claim 11 in that Jadhav et al's compounds have Gly or Leu rather than Ala at the first and last positions of their compounds. Jadhav et al teach in general that Gly, Leu, and Ala can be used in these sections of the compounds, designated by the reference as R^2, R^{2A}, R^9, and R^{9A} (see column 3, lines 30-46). It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form compounds according to Jadhav et al which have the structure of compounds of Examples 91 and 93 except that Ala rather than Gly or Leu is present in the first and last positions of each compound, because such compounds are generically embraced by Jadhav et al, because the substitution of alanine for glycine or leucine is a conservative substitution of amino acids and a homologous substitution of amino acid sidechains which would not have been expected to materially affect the activity of the compounds, and because the resultant compounds have only the HIV protease inhibitory activity which would have been expected in view of Jadhav et al.

18. Claims 7, 9, 13, and 15-22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art of record does not teach or suggest compounds having the structures recited in these claims.

19. Jungheim et al, cited in the parent PCT application, is at best duplicative of the European Patent Application '145 and Handa et al applied above.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Christopher Low can be reached at (703) 308-2923. The fax number for Art Unit 1653 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 305-7401 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1653

JRussel

December 13, 2000